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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,523	03/24/2006	Thomas W Hodge	6395-66741-06	8826

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
04/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,523	HODGE ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46,72 and 73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46,72 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed 12/22/2009 in response to the Office Action of 6/25/2009 is acknowledged and has been entered. Claim 46 has been amended. Claims 46, 72 and 73 are under examination.

Claim Rejections - 35 USC § 112

Rejection of Claims 46, 72 and 73 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendment.

New Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46, 72 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 recites "wherein the host protein is encoded by a human Rab9 target sequence". It is not clear whether the protein is encoded by Rab9 sequence itself or by some other sequence which serves as a target for Rab9. It is not clear what Applicant considers to be the Rab9 target. It is not clear whether the host proteins are the same as the target proteins. The present specification discloses: "The disclosed host sequences (including the target sequences associated with SEQ ID NO: 1-227, 229 and 231 and the proteins encoded thereby (such as SEQ ID NO: 228, 230 and 232)" page 2, lines 13-15. Clarification and/or correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46, 72 and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors deemed relevant are those of the amount of direction and the working examples provided, that quantity of experimentation necessary, the (un)predictability of the art, and the breadth of the claims.

Claims are drawn to a method of identifying a compound that decreases binding of an HIV protein to a host protein and decreases HIV infection comprising contacting the host protein with the HIV protein and the test compound, wherein the host protein is encoded by a human Rab9 target sequence and determining whether binding of the HIV protein to the host protein is

decreased in the presence of the test compound, the decrease in binding being an indication that the test compound decreases the binding of the HIV protein to the host protein, and decreases HIV infection.

Claims broadly recite any HIV protein, any host protein and any Rab9 target sequence. Applicant's specification discloses a large number of host proteins and target sequences (see [0008], [0011] and Table 1).The specification contemplates variants, fusions and fragments of the host and target proteins.

[0008] "The disclosed host sequences (including the target sequences associated with SEQ ID NOS: 1-227, 229, and 231, and the proteins encoded thereby (such as SEQ ID NOS: 228, 230, and 232), as well as variants, fusions, and fragments thereof that retain the appropriate biological activity) can mediate infection, and in some examples these host nucleic acids are required for infection. For example, the host nucleic acid can encode a cellular receptor or ligand or a fragment thereof that is recognized by a virus, such as the T-cell V-D-J beta 2.1 chain. In another example, the host nucleic acid encodes an enzyme that mediates viral infection, such as the .beta.-chimerin rho-GTPase (referred to herein as .beta.-chimerin)."

[0011] Based on the identification of several host nucleic acid and protein sequences involved in viral infection, provided herein are methods for decreasing infection of a host cell by a virus, such as HIV, Ebola, or influenza A, or treating such a viral infection, by interfering with the activity or expression of one or more host proteins shown in Table 1 (including the target sequences associated with any of SEQ ID NOS: SEQ ID NOS: 1-232, as well as variants, fragments, and fusions thereof), such as at least two host proteins, or at least three host proteins. Also provided are methods for identifying agents that can decrease viral infection of a host cell, such as infection by HIV, Ebola, or influenza."

The specification provides working examples that discuss and contemplate various general methods that could be used to practice the claimed invention, such as assays for measuring inhibition of viral infection and assays screening for agents that decrease viral infection (Examples 10-13). The specification provides working examples discussing methods for recombinant expression, disruption of gene expression, methods of treatment and methods of administration (Examples 6-9). Example 5 describes methods that can be used to decrease or

inhibit expression of genes listed in Table 1. Example 4 proposes that Rab9 decreases lipid raft formation. Example 3 describes siRNA molecules that recognize Rab9. Example 2 describes general methods for cloning sequences. Example 1 describes generation of cells with increased resistance to viral infection. There is not a single working example providing experimental data showing identification of a compound that decreases binding of an HIV protein to a host protein according to the claimed method.

The art teaches that Rab9 GTPase is required for replication of HIV type 1 (Murray et al. Journal of Virology 2005, Vol. 79. p. 11742-11751). The art teaches that Rab9 protein binds the vesicle cargo selection protein TIP47 and facilitates the transport of proteins from endosomes to trans Golgi network (Hanna et al. PNAS, May 2002, Vol. 99, p. 7450-7454, see Abstract and Discussion). The art teaches that HIV envelope glycoprotein is located in the trans-Golgi network and that Rab9 bound to TIP47 interacts with the cytoplasmic tail of the HIV envelope glycoprotein subunit p41 and is critical for the incorporation of HIV envelope glycoprotein into mature virions (Blot et al. (Journal of Virology, June 2003, Vol. 77, p. 6931-6945).

As discussed above the present claims broadly recite any HIV protein, any host protein and any Rab9 target sequence. The specification contemplates a large number of host and target proteins that can be used in the claimed method however the specification does not provide a single working example with experimental data showing identification of a compound that decreases binding of an HIV protein to a host protein according to the claimed method. The skilled artisan would be required to conduct undue experimentation in order to determine which host proteins bind HIV proteins at all, before determining which agents decrease the binding of the HIV to the host protein. The skilled artisan would be required to conduct undue amount of

experimentation in order to determine whether the decreased binding of the HIV protein to the host protein decreases HIV infection, as required by the present claims.

Thus in view of the quantity of experimentation necessary, the limited working examples, the lack of sufficient guidance in specification, and the breadth of the claims, and the unpredictability of the art with regard to decreasing HIV infection, it would take undue trials and errors to practice the claimed invention.

Claims 46, 72 and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are drawn to a method of identifying a compound that decreases binding of an HIV protein to a host protein and decreases HIV infection comprising contacting the host protein with the HIV protein and the test compound, wherein the host protein is encoded by a human Rab9 target sequence and determining whether binding of the HIV protein to the host protein is decreased in the presence of the test compound, the decrease in binding being an indication that the test compound decreases the binding of the HIV protein to the host protein, and decreases HIV infection.

Claims broadly recite a genus of HIV proteins, a genus of host protein and a genus of Rab9 target sequences. Applicant's specification discloses a large number of host proteins and target sequences (see [0008], [0011] and Table 1). The specification contemplates variants, fusions and fragments of the host and target proteins. However the specification does not provide

a representative number of species of the host proteins that bind HIV and that can be used in the claimed methods. The specification does not provide a single test compound that has the ability to decrease the binding of an HIV protein to a host protein.

The art teaches that Rab9 GTPase is required for replication of HIV type 1 (Murray et al. Journal of Virology 2005, Vol. 79. p. 11742-11751). The art teaches that Rab9 protein binds the vesicle cargo selection protein TIP47 and facilitates the transport of proteins from endosomes to trans Golgi network (Hanna et al. PNAS, May 2002, Vol. 99, p. 7450-7454, see Abstract and Discussion). The art teaches that HIV envelope glycoprotein is located in the trans-Golgi network and that Rab9 bound to TIP47 interacts with the cytoplasmic tail of the HIV envelope glycoprotein subunit p41 and is critical for the incorporation of HIV envelope glycoprotein into mature virions (Blot et al. (Journal of Virology, June 2003, Vol. 77, p. 6931-6945).

The claims are rejected because Applicant's disclosure does not provide sufficient evidence that Applicant was in possession of a representative number of species of the host proteins encoded by a human Rab9 target sequence that can be useful in the claimed method of identifying a compound that decreased HIV infection.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the specification contemplates a genus of host proteins, target proteins and HIV proteins. The specification provides a large number of host proteins and target proteins however the specification does not provide a

representative number of species of the host or target proteins that would be useful in the claimed methods. Accordingly, in the absence of insufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed structures of HIV proteins, host proteins and target proteins contemplated in the present invention and therefore conception is not achieved until reduction to practice has occurred. For the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir.1998).

The skilled artisan cannot envision the detailed structure of a genus of HIV proteins that bind host proteins that are contemplated in the invention. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures disclosed in the specification. Thus, in view of the reasons set forth above, one skilled in the art

at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claim Rejections - 35 USC § 103

Rejection of Claims 46, 72 and 73 under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (US Patent Application Publication 2003/0166870 A1) in view of Hanna et al. (PNAS, May 2002, Vol. 99, p. 7450-7454) and Muzny et al. (Accession number AC 079383, 2000, p. 1-64) as evidenced by Blot et al. (Journal of Virology, June 2003, Vol. 77, p. 6931-6945) **is withdrawn** in view of Applicant's arguments.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached at 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648